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Xylazine Test Strips for Drug Checking

Authors: Sarah Jones, Sharon Bailey

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Key Messages

Why is this an issue?

- The opioid crisis is an ongoing public health concern in Canada. In 2022, a total of 7,328 apparent opioid toxicity deaths were reported, which is an average of 20 deaths per day.
- Xylazine, referred to as tranq, is an animal tranquilizer that has appeared as an adulterant in the unregulated drug supply (particularly in opioids) and is contributing to increasing numbers of drug poisoning (overdose) events and deaths.
- There is no approved drug for humans for reversing the effects of xylazine, so detection is critical.

What is the technology?

- The Rapid Response Xylazine Test Strip by BTNX (Pickering, Ontario) is a rapid test for the detection of xylazine that can be used for drug checking in an unregulated drug supply.

What is the potential impact?

- Xylazine can have harmful effects, such as severe skin lesions, central nervous system depression, cardiovascular effects, and death.
- The detection of xylazine using a test strip could alter consumption behaviours, such as avoiding the use of contaminated drugs, reducing the quantity consumed, injecting more slowly, or choosing to use at a supervised consumption site.

What else do we need to know?

- The strips are currently available in Canada for \$349.00 for a box of 100 or \$3.49 per strip.
- Although these strips are good at checking for xylazine, they are not designed to anticipate and test for the next adulterant to enter the unregulated drug supply which could be equally or even more dangerous. Therefore, these strips would be useful as part of a robust harm reduction strategy.

New Test Strips Could Aid in Safer Consumption of Unregulated Drugs

A new test strip that can detect xylazine, a nonopioid tranquilizer appearing increasingly in the unregulated drug supply, shows promise for harm reduction. The test strips were recently approved in Canada to test urine for the presence of xylazine.¹ There is emerging evidence that these strips may also be acceptable for detecting xylazine in the unregulated drug supply. The opioid crisis claims multiple lives per day in Canada, the use of this testing device for drug checking could be a method to improve outcomes for people who use unregulated drugs.

How They Work

Xylazine is approved for use in Canada as a sedative, analgesic, and muscle relaxant for animals.² Although it is not approved for use in humans, xylazine, referred to as tranq, has appeared increasingly as an adulterant in the unregulated drug supply, especially in fentanyl or heroin.^{3,4} The Rapid Response Xylazine Test Strip (hereafter referred to as “xylazine test strips” or the “test strips”) is a rapid lateral flow immunoassay for the detection of xylazine in liquid or powder samples of a drug.⁵ This type of test strip works like other rapid assay strips. It does not need to be processed in a laboratory and provides quick results. Figure 1 depicts the test strip and the interpretation card.

Instructions for use, adapted from the BTNX demonstration video,⁶ involve:

1. Adding the sample that is to be tested to clean water and mixing until completely dissolved.
2. Submerging the test strip into the water for 5 to 10 seconds. The liquid must cover the wavy lines but not pass the solid line (refer to Figure 1).
3. Removing the strip from the sample and placing on a clean nonabsorptive flat surface.
4. Checking the results after 5 minutes. The results are **not** to be read after 10 minutes.

Figure 1: Xylazine Rapid Response Test Strip and Results Interpretation Card



Source: Image reproduced with permission from BTNX.

Who Might Benefit?

The opioid crisis is an ongoing public health concern in Canada. In 2022, a total of 7,328 apparent opioid toxicity deaths were reported, which is an average of 20 deaths per day.⁷ Adulterants to the unregulated drug supply, such as fentanyl and xylazine, are contributing to the increasing numbers of drug poisoning (overdose) events.² Xylazine is not approved for use in humans and can have harmful effects, such as severe skin lesions, central nervous system depression, cardiovascular effects, and death.⁸ According to preliminary data from the Office of the Chief Coroner of Ontario, xylazine was present in 2% to 4% of opioid-related deaths between Q4 2021 to Q3 2022.⁸ Xylazine is particularly dangerous because it is not an opioid; therefore, other methods of treating drug poisonings, such as naloxone, are not effective.² The dose of xylazine required for toxicity in humans is between 40 mg and 2,400 mg. However, if there are many adulterants in a particular drug sample, it may be difficult to determine whether it was the presence of xylazine alone or in combination with other adulterants that resulted in the poisoning fatality. Concentrations of xylazine in fatal poisonings cases have been recorded anywhere from trace amounts to 16 mg/L. This may be because even small amounts of xylazine increase the effects of other drugs, such as heroin.⁹ The substantial overlap between fatal and nonfatal doses indicates that there is no “safe” blood concentration of xylazine.⁹ It is difficult to predict whether the amount of xylazine in a sample will result in a fatality.

Xylazine test strips are well-suited for a harm reduction role in the form of drug checking. Drug checking can be done by an individual on their own before drug use or as part of a drug checking program.¹⁰ Drug checking programs allow individuals to anonymously submit drug samples for analysis and to receive individualized and fact-based consultation regarding their samples.¹¹ These programs have been associated with safer consumption behaviours, such as avoiding the use of contaminated drugs, reducing the quantity consumed, injecting more slowly, or choosing to use at a supervised consumption site.¹² Drug checking programs and pilots have operated either at the point of care (where an individual can have a sample checked onsite, such as at a testing centre, community outreach centre, or safer consumption site)¹¹ or through a drop off–pick up model in which samples are dropped off at a convenient time and results are communicated once the checking has been completed.¹¹

Availability in Canada

The test strips were approved for use in Canada in April 2023 for the detection of xylazine in urine samples.¹ They are also available for use as a consumer product for drug checking purposes.

What Do They Cost?

The strips are currently available in Canada for \$349.00 for a box of 100 or \$3.49 per strip (Khasim Ali Khan, Technical Operations Director, BTNX, Pickering, ON: personal communication, May 26, 2023). The company has stated there may be an alternative price available for nonprofit organizations that order this product.¹³ As

of this writing, xylazine test strips are more expensive than other drug checking test strips (e.g., fentanyl test strips are available for US\$100 for a box of 100 strips).¹⁴

The cost-effectiveness of drug checking programs is not clear. There is evidence that confirms the cost-effectiveness of other harm reduction strategies, notably supervised consumption sites where drug checking may be offered. The cost-effectiveness of those programs has been calculated in terms of serious infections avoided.¹⁵ Researchers have called for work that examines the cost-effectiveness of test strip distribution.¹⁰

Current Practice

Harm reduction is a multipronged approach comprising “policies and programs which aim to reduce the health, social, and economic costs of legal and illegal psychoactive drug use without necessarily reducing drug consumption.”¹⁶ The Supreme Court of Canada ruled in 2011 that harm reduction services are health care.¹⁶

A robust harm reduction strategy involves many components, including (but not limited to):

- safer consumption sites
- wide distribution of naloxone
- opioid-agonist therapy
- safer supply programs
- drug checking.¹⁷

Although there is no national guideline on drug checking practices, there are many guidelines created by community agencies that outline the reasons to perform drug checking as well as information about how to set up drug checking services, including information about the technologies available (including test strips) as well as the training required for technicians, site set up, and procedures.^{11,18,19} The guidance documents on drug checking programs do not include information specific to xylazine test strips likely because this is an emerging area of interest in Canada.

What Is the Evidence?

A study from Philadelphia published in March 2023 aimed to assess the performance of the test strips for drug checking purposes.²⁰ This laboratory study tested materials provided through public health partnerships and validated the results by testing lab-created controls. The “real-world” materials were materials used in unregulated drug consumption. These materials were tested by both gas chromatography–mass spectrometry and liquid chromatography quadrupole time-of-flight mass spectrometry to confirm the presence of individual drug components as well as the presence and quantity of xylazine, fentanyl, and other adulterants.²⁰ The performance of the xylazine test strips was deemed acceptable for drug checking purposes; the strips demonstrated high sensitivity (100%), specificity (85%), and precision (91%). Lidocaine was identified as an interferent that may lead to false-positive results.²⁰

Early results from the John Hopkins Bloomberg School of Public Health regarding the use of the xylazine test strips for drug checking show the overall sensitivity of the test strips to be good and cross-reactivity to be limited to a single compound – lidocaine.²¹ The xylazine test strips were found to detect xylazine at concentrations as low as 0.5 mcg/mL in solution and consistently produced a positive result at concentrations as low as 2.5 mcg/mL.²¹ When the xylazine test strips were used to detect xylazine in real-world drug residue samples, xylazine was consistently detected in samples with a concentration greater than 2 mcg/mL; there were mixed results when the concentration ranged between 0.1 mcg/mL and 2 mcg/mL.²¹ These findings about the limitations of these test strips in the smallest concentrations are pertinent to the overall effectiveness of the strips to detect xylazine in the unregulated drug supply. These results plus the findings from the study in Philadelphia suggest the BTNX test strips are a good tool for drug checking programs.

Safety

The studies summarized in this report are not in vivo studies, which means the test strips were not tested on people. Rather, the studies tested how well and how often the test strips detected xylazine in a variety of substances. One potential safety concern outlined by the studies was the inconsistent detection of lower concentrations of xylazine (i.e., amounts lower than 2.5 mcg/mL).²¹ It is possible that a substance that tests negative for xylazine using 1 of these strips might in fact contain a small amount of the substance. Because there is no safe blood concentration of xylazine for humans, more research is needed to determine the level of risk posed by missing smaller concentrations of xylazine for people who use drugs.

Issues to Consider

Another drug checking method is Fourier transform infrared (FTIR) spectroscopy. Compared with FTIR, immunoassay test strips, such as the xylazine test strips, are faster, easier to read, are portable, and are able to be used almost anywhere (whereas spectrometers require space and a power source). However, the test strips are designed to detect the presence of only 1 substance, whereas FTIR can detect a wide range of compounds and even provide a percentage estimate of the components within a substance.¹¹ Each procedure has strengths, which makes both types of testing useful in different drug testing settings depending on need.

Across jurisdictions, the regulatory and product development pathways for these types of devices are not always clear.¹² For example, xylazine test strips do not require Health Canada approval to be used for drug checking purposes because they do not meet the definition of an in vitro diagnostic device when used in this manner. The strips have received approval for checking urine samples for the presence of the drug. Similarly, in the US, test strips used to analyze drugs before consumption do not meet the definition of an FDA-regulated device. Therefore, these devices have not been reviewed or authorized by the FDA, although they are widely used for drug checking purposes in the US.¹² Innovation in the regulatory space may be helpful in removing barriers and ensuring the safety of individuals who use these test strips for drug checking.

There is evidence that take-home fentanyl test strips for individual drug checking can provide similar results as formal drug checking programs.¹⁰ A practical limitation of these test strips is what an individual chooses to do when they get a positive result. In some cases, an individual may make the decision not to use from that supply or choose not to use the drug while alone but rather at a safer consumption site. However, if there is no safer alternative supply, simply having the information about the presence of adulterants may not be sufficient to change behaviour.

Related Developments

Drug checking and test strips are a growing field and market. The manufacturer of the xylazine test strips, BTNX, also produces fentanyl test strips for harm reduction as well as a number of single-drug test strips, including 1 that tests for benzodiazepines in urine.²² It is unclear at this time whether the company will be developing additional tests or combination test strips as new adulterants present in the unregulated drug supply.

Due to the known harms and prevalence of xylazine in the unregulated drug supply, there is ongoing research to support the detection of this substance. One device is a laser-scribed graphene device fabricated on a polymeric polyetherimide substrate to detect xylazine in beverages and synthetic urine samples.²³ The manufacturers of this device state that it is a low-cost, single-use system.²³ A study that compares this device with more standard testing would be useful.

At a health systems level, there is evidence that rolling out drug checking programs that span multiple communities could be beneficial in many ways. This type of program was started in Massachusetts, with a statewide drug checking program that was able to share information about adulterants in the unregulated supply throughout the state. This type of program could be beneficial to both the people who use drugs and health care decision-makers when planning and deploying additional harm reduction strategies.²⁴

Looking Ahead

Unlike opioid poisonings that can be treated with naloxone, there is no approved drug for reversing the effects of xylazine for humans. Treatment for an apparent xylazine poisoning is supportive care: supporting breathing and blood pressure.⁹ There are a few drugs known to reverse some of the effects of xylazine in animals; however, additional research is needed to determine if these drugs could be approved for use in humans.⁹

A notable limitation of these strips is that adulterants to the unregulated drug supply come and go. Although these strips are good at checking for xylazine, they are not designed to anticipate and test for the next adulterant to enter the unregulated drug supply that may be equally or even more dangerous. Because of the changing nature of the unregulated drug supply, drug checking using xylazine test strips should be considered 1 part of a more robust harm reduction program including multiple strategies, such as safer consumption sites, distribution of naloxone, opioid-agonist therapy, and safer supply programs.

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Appendix 1: Methods

Literature Search Strategy

An information specialist conducted a literature search on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were xylazine, harm reduction, and test strips. Where possible, retrieval was limited to the human population. The search was completed on June 1, 2023, and limited to English-language documents published since January 1, 2018. Internet links were provided, where available. Regular alerts updated the database literature searches until the publication of the final report.

Study Selection

One author screened the literature search results and reviewed the full text of all potentially relevant studies. Studies were considered for inclusion if the intervention was BTNX rapid response xylazine test strips. Conference abstracts, preprints, and grey literature were included when they provided additional information to that available in the published studies.